Implementing lung health interventions in low- and middle-income countries:

Implementing lung health interventions in low- and middle-income countries – a FRESH AIR systematic review and meta-synthesis

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Take home message: This systematic review and meta-synthesis shows why implementation of lung health interventions often fails in low-and middle income countries, and it provides critical factors to prevent failure with their level of evidence.

Abstract

The vast majority of patients with chronic respiratory disease live in low- and middle-income countries (LMICs). Paradoxically, relevant interventions often fail to be effective particularly in these settings, as LMICs lack solid evidence on how to implement interventions successfully. Therefore, we aimed to identify factors critical to the implementation of lung health interventions in LMICs, and weight their level of evidence.

This systematic review followed Cochrane methodology and PRISMA reporting standards. We searched eight databases without date- or language restrictions in July 2019, and included all relevant original, peer-reviewed articles. Two researchers independently selected articles, critically appraised them (using CASP/MetaQAT), extracted data, coded factors (following CFIR), and assigned levels of confidence in the factors (via GRADE-CERQual). We meta-synthesized levels of evidence of the factors based on their frequency and the assigned level of confidence. (PROSPERO:CRD42018088687)

We included 37 articles out of 9111 screened. Studies were performed across the globe in a broad range of settings. Factors identified with a high level of evidence were 1) *Understanding needs of local users*, 2) ensuring *Compatibility* of interventions with local contexts (cultures, infrastructures), 3) identifying influential stakeholders and applying *Engagement* strategies, 4) ensuring adequate *Access to knowledge and information*, and 5) addressing *Resource Availability*. All implementation factors and their level of evidence were synthesized in an implementation tool.

To conclude, this study identified implementation factors for lung health interventions in LMICs, weighted their level of evidence, and integrated the results into an implementation tool for practice. Policymakers, non-governmental organizations, practitioners, and researchers may use this FRESH AIR Implementation tool to develop evidence-based implementation strategies for related interventions. This could increase interventions' implementation success, thereby optimising the use of already-scarce resources and improving health outcomes.

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Data sharing: All data and meta-data can be shared upon reasonable request. This includes the study protocol, meeting minutes describing considerations for data analysis. Within reasonable time after email request data will be shared via a secure webbased system.

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Introduction

Chronic respiratory diseases (CRDs) are a silent and growing epidemic in low- and middle-income countries (LMICs). COPD is now the third leading cause of death worldwide; over 90% of these deaths and 80% of asthma-related deaths occur in LMICs.[1-5] LMICs are disproportionately burdened by CRDs because of the early and high exposure to risk factors for lung impairment.[6-13] Suboptimal access to diagnostic- and treatment options in LMICs additionally exacerbates disease severity.[6, 11] Although promising interventions targeting CRD have existed for decades, many fail to translate into meaningful health outcomes. The disappointing intervention effects are often attributed to implementation failure.[14-18] In some estimates, over 60% of organizations' implementation efforts are unsuccessful.[19] Implementation success of clean cookstove programmes is often reported as strikingly low, with stove adoption rates of 4-10%.[20-25]

However, implementation – the act of carrying an intervention into effect[26] – is complex. Throughout the entire implementation process, from the dissemination of an intervention to its sustained use,[27] numerous factors determine success or failure. These implementation factors are often interacting and influential at multiple levels. To better understand the factors so that they can be adequately addressed in implementation strategies, factors can be pragmatically structured. The Consolidated Framework for Implementation Research (CFIR) integrated 42 implementation factors from existing implementation theories,[18] and categorised them in five domains: 1) innovation characteristics (e.g. the adaptability of an intervention); 2) outer setting (e.g. understanding the needs of local users); 3) inner setting (e.g. resource availability); 4) characteristics of individuals (e.g. self-efficacy); and 5) process (e.g. engagement of stakeholder). The importance of each factor depends on the context.[28, 29] Hence, implementation strategies are more successful when context-specific factors are known and addressed.

Therefore, it is essential to understand which specific factors play a role in the context of CRDs in LMICs. Paradoxically, despite the highest burden of CRD in LMICs, precisely in these countries evidence on what factors determine implementation success is limited, fragmented and of varying methodological quality.[30-33] Extrapolating the evidence from high-income countries to LMICs is inappropriate because of differences in health, economic, and cultural contexts. Several calls already highlighted the need for high-quality implementation research in LMICs.[25, 34-37] Therefore, in this study, we aimed to identify factors critical to the successful implementation of interventions targeting CRDs in LMICs, and to weight their level of evidence.

Methods

This systematic review and meta-synthesis is part of the Horizon2020 FRESH AIR project (Free Respiratory Evaluation and Smoke-exposure reduction by primary Health cAre Integrated gRoups), addressing the implementation of prevention, diagnosis, and treatment of CRD in low-resource settings (trial registration number: NTR5759).[38] This review is registered at PROSPERO (CRD42018088687) and follows Cochrane methodology[39, 40] and the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) reporting standards.[41]

All steps of the review process were performed by two researchers (EB & DV) independently. Results were compared, and discrepancies solved through discussion. A third researcher (RvdK) was consulted when consensus could not be reached. We systematically applied validated tools throughout the entire process, to enhance the reproducibility and transparency of our outcomes (Figure 1).

Search strategy and selection criteria

We developed the search strategy together with a certified medical librarian; it contained (synonyms of) implementation, LMICs, and CRD or specific relevant interventions such as 'smoking cessation' (Appendix 1). We focused on asthma and COPD as the most prevalent chronic lung diseases. In PubMed, Embase, Global Health Database, Cochrane, PsycINFO, Emcare, Web of Science, and CINAHL we searched without language restriction for articles published by Oct 23, 2017, and updated our search on July 10, 2019. We included all relevant, original, peer-reviewed articles focusing on the implementation of interventions targeting CRD in LMICs (as classified by the World Bank[42]). As recommended for studying implementation, quantitative, qualitative, and mixed-method articles were considered relevant.[26] Articles were excluded if they focused on legislation at a national

governmental level (e.g. implementation of tobacco taxes) or on hypothetical interventions (e.g. theoretical willingness to adopt an intervention), if no factors were reported, or if no full text was available after contacting the authors. Our orienting search resulted in a disproportionate number of articles on the implementation of clean cooking interventions targeting household air pollution. To avoid this specific intervention dominating all review findings, we decided to split our review into two parts. This first review regards the implementation of all but clean cooking interventions, while the second (to be published later) will be exclusively dedicated to those.
Full operationalisation of the search criteria is presented in Appendix 1. In addition, we manually searched Google and Google Scholar for the full articles from identified conference abstracts and study protocols, and screened all references from relevant reviews and the included articles.

Critical appraisal
To critically appraise the included articles on relevance, reliability (reporting quality), validity and applicability, we used the validated Meta Quality Appraisal Tool (MetaQAT)[43] (Appendix 2), and as recommended we embedded the Critical Appraisal Skills Programme (CASP) into it.[44] Results served as input for the assessment of level of evidence of the identified factors (see data-analysis).

Data extraction
We extracted descriptive study characteristics (author, year, study design, country, setting/population, intervention, type of outcomes measures used, and funding source) and the implementation factors using a pilot-tested, standardised sheet. Speculations (such as 'Factor A might have influenced implementation') or repetitions in the reporting of factors within the same article were not extracted. We extracted modifiable factors (e.g. factors to address user demographics would be extracted, but demographics on their own would not), to serve the design of future implementation initiatives. Only factors based on original data were extracted. If several articles were based on the same study, we compared the article's aim, methods and results in detail. If these were similar, we extracted data from the article that scored highest in our appraisal. If they differed (e.g. one was a pilot version and the other the scale-up of the same study), data from both (or more) articles were used.

Data analysis
For our meta-synthesis (weighting of the factors) we used content analysis, in which all data are categorised into themes and the frequencies of the themes are determined. Content analysis is suitable for both qualitative and quantitative evidence.[45]
First, we categorised all identified implementation factors by deductive coding using the CFIR.[18] We inductively added several codes to the CFIR (such as 'language' or 'role model') when our extracted factors did not match existing codes (Appendix 3). Second, we used the Grading of Recommendations Assessment, Development and Evaluation-Confidence in the Evidence from Reviews of Qualitative research (GRADE-CERQual) tool to determine the level of confidence in the importance of the coded factors. The GRADE-CERQual tool has four components (Figure 1), and the results of the critical appraisal served as input for scoring those (e.g. a high MetaQAT score for relevance translated into 'no to very minor concerns' in the GRADE-CERQual component 'relevance').[46] Third, each factor was awarded a maximum of four points per component per study in which it appeared (four points for 'no to very minor concerns' regarding the component in that specific study, three for 'minor concerns', two for 'moderate concerns', and one for 'substantial concerns'). Hence, factors were awarded higher scores when they appeared in more studies (the principle of content analysis), and when the components methodology, relevance and adequacy of the study were appraised as high. The fourth GRADE-CERQual component 'coherence' was not rated, because the number of studies in which the factor appeared already accounted for coherence. To conclude, the higher a factor scored, the higher the level of evidence to regard it as an important factor.

Role of the funding source
This study was funded by the EU Research and Innovation program Horizon2020 (Health, Medical research and the challenge of ageing) under grant agreement no. 680997. The funders had no role in study design, data collection, data analysis, data interpretation, or writing of the report. All authors had full access to all the data and EB, DV, RvdK and NC, the guarantor, had the final responsibility for the decision to submit the study for publication.

Reflexivity
Members of our research team came from diverse backgrounds (researchers and clinicians from psychology and medicine, with work experience in high-income countries, LMICs, or both). In these roles, we had experienced working conditions characterised by many of the factors we identified, such

as lack of resources and personnel. We recognised that we were potentially more receptive to factors we had experienced ourselves, so adhered to our standardised extraction procedures.

Results

Search results

Our search resulted in 9111 unique articles. After full-text screening we included 37 articles derived from 33 different studies (Figure 2, Table 1). One article was excluded from the analysis,[47] as its factors were based on the exact same study data as another article which scored higher in the critical appraisal.[48]

Study characteristics

The studies resulting from our search were conducted in 17 different LMICs across five geographical regions: Latin-America (Brazil,[49-53] the Dominican Republic,[54] Mexico,[55] Surinam[56]), Africa (Malawi,[57] South-Africa[58-60]), the Middle East (Lebanon[61], Syria[62]), Asia (China,[63-67] India,[47, 48, 68-73] Indonesia,[71, 74] Malaysia,[75] Nepal,[76, 77] Pakistan,[78] Russia,[79] Thailand[80-82]), and Oceania (Fiji[83]) (Table 1, Figure 3). Most studies were based in healthcare settings (n=17; primary care (n=9), secondary care (n=5), primary/secondary care combined (n=3)), followed by schools (n=13), and the community (n=6). The majority of the study interventions focused on tobacco (n=27; cessation (n=10), prevention (n=8), both (n=2) and control (i.e. smoking-free setting) (n=7)). Three studies focused on interventions to improve the implementation of guidelines. One study focused on quality improvement of COPD management, one on delivery of integrated asthma/COPD care, and one on the adaptation of post-partum rituals using biomass smoke to 'protect' newborns. Three articles used quantitative methods for determining implementation factors, 31 used qualitative methods, and two used both.

Critical appraisal of the studies

The quality of the articles varied: 19 articles scored high in the MetaQAT on relevance to the research question, 17 scored medium and one scored low (Table 1, and for further details Appendix 4). Articles scored variably on reliability (15 high, 11 medium, 11 low) and the lower scores were often due to unclear reporting of methods. Data analyses and researcher reflexivity were particularly poorly reported in many qualitative articles, which affected the reproducibility and transparency (thus validity). Twelve articles scored high on validity, ten scored medium, one scored low and for 14 articles validity was unclear.

Implementation factors

Forty-five implementation factors were identified, with a large variation in factors' levels of evidence (Appendix 5). The factors with the highest level of evidence are described in further detail below, these belonged to CFIR domains *Process*, *Inner setting*, and *Outer settings* (Figure 5). A full overview of all weighted factors, their definitions, and illustrations of how they occurred in the included studies is detailed in Appendix 6.

Engaging – 'attracting and involving appropriate individuals in the implementation and use of the innovation (…)'[18] – in the domain *Process* was coded 72 times across 29 articles. Identifying influential stakeholders before and during the implementation process, and developing effective engagement strategies was often reported as 'crucial'. Moreover, authors stated that the context determined who was considered as influential. The articles addressed relevant deliverers (e.g. teachers, staff, health workers), potential collaborators (e.g. government officials, village leaders, or other authorities who could block implementation if not successfully engaged) and recipients of the intervention (e.g. 'all villagers at once' vs 'initially only highly respected villagers') as important stakeholders to consider. Among a broad range of reported strategies, engagement was frequently established after gaining trust and commitment from the participants, and when a sense of ownership was created (e.g. through participatory approaches). Equally, failure to engage stakeholders was attributed to the lack of engagement activities, e.g. demotivation of intervention recipients due to lack of ongoing communication.

Compatibility was another factor with a high level of evidence, coded 48 times across 23 articles. Categorised in the subdomain *Implementation Climate* (domain *Inner setting*), compatibility is defined as the degree of fit between meaning and values attached to the innovation and of the involved individuals, and how the innovation fits with existing workflows and systems.[18] Implementation success was often attributed to embedding interventions into local, existing infrastructures (e.g. the

primary care infrastructure), carried out by people in already established networks (e.g. community health workers), and when aligned with local cultural values. This can, for example, be achieved in highly participant-centred interventions. "*Perhaps the most important lesson was eventually letting go of some of our own techniques and agendas and allowing an indigenous culture to develop their own program."* The local participants developed their own programme and implementation strategy, aligned with their local context, and hence, implementation was highly successful.[83]

The second important subdomain in the domain *Inner setting* was *Readiness for implementation* (coded 76 times across 32 articles), of which *Access to knowledge and information* (28 times, 22 articles) and *Available resources* (37 times, 21 articles) were defining factors. Studies generally reported the lack of these factors as implementation barriers. Particularly training in knowledge and skills (e.g. knowledge on risks to lung health or motivational interviewing skills) were reported as insufficient, including lack of access to educational materials. The most commonly lacking available resources were time and personnel. Other notable resources lacking were limited physical space (such as crowded consultation rooms), insufficient materials (medication, equipment), or assets (electricity). Funding to overcome these barriers was often not feasible, but authors reported that the (lack of) resources should always be considered in the implementation strategy. Where possible, adaptations can then be made accordingly.

Another notable factor was understanding and accurately prioritising on the *Needs of local users* (*Outer setting*). For example, deliverers in one study realised that Chinese parents did not necessarily feel a need for smoking cessation. They also recognised the parents' need for connecting with their child (and children had a unique position in the Chinese one-child families). Deliverers then educated the children on smoking and cessation, which eventually helped to motivate their parents to quit.[64] Level of evidence was also high for *Cosmopolitanism* (networks of the organization with external organizations; *Outer setting*) and *Networks and Communications* (*Inner setting*).

Notably, all factors appeared strongly interrelated; e.g. engaged stakeholders provided adequate knowledge about the needs of those served by the organization, which improved compatibility, which in turn increased the perceived advantage of the intervention, etc. Also, when comparing the implementation factors and their level of evidence across the geographical regions, findings were highly similar.[1] Only for China, factors related to the *Outer setting* (e.g. *External policies and incentives*) were reported less frequently compared to the other regions.

To facilitate future implementors in the translation of the comprehensive overview of all factors to practice, we summarised the factors in a practical, simplified, and manageable implementation tool (Figure 5 and Appendix 7). The tool contains factors prioritised by their level of evidence, and illustrates those factors with examples of how to address them.

[1] We compared Latin-America, Africa and Asia (China and India were considered both individually and as part of Asia). The Middle East (n=2) and Oceania (n=1) were not considered because of the small number of studies.

Table 1. Characteristics of the included studies and critical appraisal, by author

Author	Study design	Country	Setting; population	Intervention	Summary of appraisal			
					Rv	R	V	A
Aghi, 2016*[1]	Qualitative study within an RCT	India	Public urban and rural schools; health educators, lead teachers and staff	Tobacco cessation	+	-	-	/
Aldinger (IUHPE – Promotion & Education, 2008*[2]	Qualitative (institutional ethnography)	China	Primary to vocational schools; administrators, staff, teachers, students, and parents	Tobacco prevention within programme of health-promoting schools	/ 1	/	/	+
Aldinger (Health Education Research, 2008*[2]	Qualitative (institutional ethnography)	China	Primary to vocational schools; administrators, staff (such as school doctors), teachers, students and parents	Tobacco prevention within programme of health-promoting schools	-	+	/	+
Asfar, 2016	Qualitative study within an RCT	Syria	Primary healthcare setting; physicians and medical students	Tobacco cessation	+ 1	-	?	/
Assanang-kornchai, 2014	Qualitative (action research)	Thailand	Primary healthcare setting; healthcare workers (nurses, administrators, directors)	Tobacco, alcohol, and substance use screening and brief intervention	/ 1	/	/	+
Bheekie, 2006	Qualitative study preparing for an RCT	South Africa	Primary healthcare setting; trained nurses, with a supervisory position as care coordinators	Train-the-trainer programme on implementation of respiratory guidelines on (obstructive) lung diseases	+	+	+	/

Bteddini, 2017	Mixed-method, with quantitative survey and participatory approach for qualitative data	Lebanon	7 public and 7 private schools throughout the country; trained external facilitators training 10 sessions for 844 students	Waterpipe smoking prevention/delay of starting to smoke	− + + + 1
Castaldelli-Maia, 2017	Qualitative	Brazil	Urban psychosocial care units (primary care) across the country; diverse health professionals (e.g. dentist, nurses, physicians, managers)	Tobacco cessation	+ − ? − 1
Chatterjee, 2017	Qualitative	India	Rural villages; community members (programme managers, coordinators, health workers and stakeholders at village level)	Tobacco-free village	+ − − + 1
Cruvinel, 2013	Quantitative, survey design (correlations)	Brazil	Urban, primary healthcare; 149 diverse workers (e.g. community health workers, nurses, physicians)	Training on tobacco, alcohol and drug use screening and brief intervention	− + + −
Elsey, 2016	Mixed-method, factors derived from qualitative data (action research)	Nepal	Urban and rural primary healthcare; patients, healthcare providers, managers and policy makers	Tobacco cessation - Behaviour support	+ + + + 1
Goenka, 2010*[3]	Mixed-method study within an RCT	India	32 Urban, public & private schools; professionals with a master in psychology, sociology, or nutrition who taught teachers and peer leaders	Tobacco prevention by teachers and peer-leaders	− + − −
Groth-Marnat, 1996	Qualitative	Fiji	Traditional village; community members	Tobacco cessation	+ − ? − 1
Ishaak, 2014	Mixed-method, factors derived from qualitative data	Suriname	Urban junior high school; management and teachers	Tobacco and other drug prevention	− − − −
Khan, 2019	Mixed-method, embedded in RCT, factors derived from qualitative data	Pakistan	30 Primary and secondary level public healthcare facilities; care providers (15	Integrated COPD/asthma care	+ + + + 1

			received intervention, interviews in 4 of the centres)		
Malan, 2015	Qualitative	South Africa	Primary care practice; care providers (nurses and physicians)	Brief behaviour change counselling (5A's) for tobacco, diet, physical activity and alcohol abuse	⊘ + + + 1
Marsiglia, 2014	Qualitative for the factors reported, within a quantitative study	Mexico	Urban public middle schools; teachers	Tobacco and other substance use prevention	⊘ - ? -
Mash, 2010	Qualitative, prospective (outcome mapping)	South Africa	Urban and rural, primary care to specialised care with a focus on the public sector; doctors, clinical nurse practitioners, pharmacists, National Council for Medical Schemes, the Department of Health, universities and training bodies patients	Asthma-guideline implementation and dissemination	+ ⊘ ? ⊘ 1
McAlister, 2000	Qualitative for the factors reported, within a quantitative study	Russia	Community level; hospital staff, intervention for community smokers	Stop smoking campaign	+ ⊘ ? ⊘
Medeiros, 2016	Mixed-methods, factors derived from qualitative data	Brazil	Urban schools; teachers, school administrators, coaches, other stakeholders (e.g. municipality) and students	Tobacco prevention within a drug use prevention programme	⊘ + + +
Mehanni, 2019	Qualitative	Nepal	Small rural hospital (managed through a public-private partnership)	Quality improvement initiative for management of COPD	+ - ? ⊘
Melson, 2017	Mixed-methods within pilot RCT; factors derived from qualitative data (quantitative data n.a., regard hypothetic factors prior to implementation). Pro- and retrospective	Malaysia	Secondary school; students	Peer-led anti-smoking intervention (smoke-free class)	+ + + + 1

Nagler, 2012*[1]	Qualitative, formative pilot study preparing for an RCT	India	One public urban and one rural school, not included in the RCT; health educators and teachers	Tobacco cessation – school based	⊘ + + ⊘
Nichter, 2010	Qualitative	India & Indonesia	Lead public & private medical schools and outreach to their communities	Training network for tobacco prevention (curricula), outreach and clinic on smoking cessation	+ - ? ⊘ 1
Ossip, 2016	Qualitative (Rapid Assessment Process)	Dominican Republic	Urban, peri-urban & rural communities with active Community Technology Centers; a multidisciplinary team including specialists of psychology, anthropology, nursing, epidemiology, statistics and public health (from the US) and medicine (DR)	Tobacco cessation – participatory approach	+ ⊘ ? ⊘ 1
Pawar, 2015*[1]	Qualitative factors reported within a quantitative study, embedded in an RCT	India	72 Public urban and rural schools; health educators, lead teachers and staff	Tobacco cessation - lay interventionist teaching teachers	⊘ - ? -
Pereira, 2016	Quantitative, population-based cross-sectional survey design	Brazil	Urban public and private schools; 263 school managers (headmasters, pedagogical coordinators, coordinators of the prevention programmes)	Tobacco prevention within a drug use prevention programme	⊘ + ⊘ ⊘ 1
Perry, 2008*[3]	Qualitative study (translational research) within an RCT following translational research	India	32 urban schools, half were public and half were private; school administration, teachers, and peer-leaders	Tobacco prevention	⊘ - ? ⊘ 1
Persai, 2015	Qualitative	India	At district level; senior district officials	Tobacco control	⊘ + + + 1
Portes, 2014	Qualitative, retrospective	Brazil	Urban primary healthcare units in a medium-sized municipality; municipal programme coordinator, and senior health professionals trained on smoking cessation or local managers	Tobacco control – training healthcare professionals on facilitating treatment & prevention activities	+ + + + 1

				(Furthermore, interventions on governmental level, n.a. to our study)	
Prasodjo, 2015	Mixed-method, factors derived from qualitative data (amongst which participatory action research)	Indonesia	Rural community; local institutions (policy makers, medical staff, community leaders and other stakeholders)	Post-partum smoke ('Sei') traditions – Behavioural change communication campaign targeting household air pollution	+ - / /
Rosati, 2012	Mixed-methods, factors derived from qualitative data	Thailand	Urban family setting; health educators towards families	Tobacco, alcohol and other substance abuse prevention, sex education	/ / / / 1
Sodhi, 2014	Mixed-methods, factors derived from qualitative data	Malawi	30 urban and rural, government funded and non-government funded health centres; primary healthcare workers: clinical officers, medical assistants, and nurses	Train-the-trainer on guideline use for providing integrated primary lung healthcare	/ / / + 1
Vitavasiri, 2010	Quantitative questionnaire	Thailand	676 Thai hospitals; personnel	Smoke-free hospitals	+ - ? - 1
Wang, 2008	Qualitative	China	County-level hospitals; health professionals, hospital president, director of preventive health, representatives of the hospitals	Smoke-free hospitals	+ + + + 1
Xiao, 2013	Mixed-method, factors concerned qualitative data	China	41 Hospital across the country, the majority from a tobacco control network; medical doctors and directors	Smoke-free hospitals	/ - ? + 1
Ziedonis, 2012	Qualitative	China	Hospital-based mental health centre; personnel and patients	Smoke-free hospitals	+ - ? / 1

Studies were prospective unless otherwise indicated. Rv = relevance, R = reliability, V = validity, A = applicability to a wider public health context. RCT = randomised controlled trial. + High / Medium - Low ? Unclear score in appraisal. Relevance 1 = Evaluation of implementation was a primary outcome of the article. *Articles from the same study. *[1]Findings from Aghi et al. were excluded from the analysis, as Pawar et al. based their findings on the same study data and had higher appraisal scores. Nagler et al. based findings on a different study data (pilot study) and was included. *[2&3]Findings from both studies were included as these were based on different study data.

Discussion:

Main results

In this systematic literature review and meta-synthesis, we identified and weighted factors critical to the implementation of interventions targeting CRD in LMICs. Factors for which the level of evidence was high were 1) understanding needs of local users, 2) compatibility of the intervention with the local context (such as the political- and health infrastructure or the culture), 3) identification of influential stakeholders and application of engagement strategies, 4) adequate access to knowledge and information (including skills), and 5) sufficient available resources. Additional factors were identified with a lower level of evidence. Most important recommendations for future implementors were compiled in the FRESH AIR Implementation Tool.

Strengths and limitations

To the best of our knowledge, this systematic review is the first to focus on factors critical to the implementation of diverse CRD-interventions. It focused on LMICs, precisely where the burden of disease is highest, while evidence is fragmented and often poor for these settings. This review had a rigorous design and conduct, following Cochrane methodology and PRISMA reporting standards.[39-41] Every step was standardised and performed independently by two researchers. Validated tools were applied at each stage,[18, 43, 44, 46] with a transparent description of their operationalisation. Moreover, we adopted a comprehensive approach with an extensive search in eight databases with no language/date restrictions. We synthesised real-world evidence from highly diverse settings and countries in the included studies, resulting in a high generalisability of the findings to other settings.[84] In fact, the LMICs in this review were broadly representative of the population distribution across the worlds' continents, among others with many studies conducted in China and India.

However, several relevant types of interventions were underrepresented or even absent in the implementation literature, such as patient education, self-management, or pulmonary rehabilitation. Due to the small number of existing studies that focus on such interventions, we were unable to assess whether their implementation factors meaningfully differed from tobacco-related interventions. However, as the desired implementation behaviour is focussed on a similar health goal in similar settings, we assume that there will be at least some overlap in implementation factors. Meanwhile, the high representation of tobacco-related studies in literature remains welcome, with 80% of the world's smokers living in LMICs.[85] As another limitation, we recognise along with other authors that implementation studies are poorly indexed and we possibly missed relevant studies.[86] Yet, data saturation was still achieved in the identified factors and the hierarchy of their level of evidence. Notably, absence of evidence (factors not reported) should not be interpreted as evidence of absence (factors not important);[45] we could only determine the level of confidence in the importance of factors, for which we relied on the existing evidence.

Comparison to previous literature

Our findings partly overlap with implementation factors considered important for clean cooking interventions as reported in two reviews.[87, 88] First, our factors 'Compatibility' and 'Understanding local users' needs' correspond to 'user needs' (e.g. the ability of clean cookstoves to give the food the right taste or save fuel). Second, our factors 'Engaging' and 'Access to knowledge and information' correspond to 'community involvement' and 'user training'. The authors of these studies similarly observed that barriers could turn into facilitators when these are adequately addressed and vice versa. They also concluded that factors should be addressed simultaneously because they all interrelate. The overlap between their findings and ours may not be surprising, as clean cooking interventions similarly target CRD in LMICs. Possibly, this supports the assumption mentioned earlier that implementation factors would not differ substantially for those chronic lung health interventions in LMICs that have not yet been studied.

Implementation is a relatively unexplored topic in LMICs, and we predominantly relied on qualitative articles. Qualitative studies allow for a deeper understanding of the *how, what and why* of implementation processes.[89] As opposed to in quantitative studies, the concept 'high level of evidence' cannot be quantified or tested on significance in qualitative studies. Therefore, a combination of qualitative with quantitative (mixed-method) evidence would be highly welcome; such studies are still largely unavailable. The need for more high-quality implementation evidence for LMICs has been highlighted repeatedly.[25, 34-37, 90] Systematic reviews are particularly scarce.

Interpretation and implications for implementation initiatives

Our findings could serve future implementation initiatives, especially those initiatives targeting CRD in LMICs. To facilitate the design of effective implementation strategies for CRD-related interventions, we have developed a comprehensive overview of all implementation factors, their level of evidence, and examples of how they played a role in the included studies (Appendix 6). In addition, we translated factors from the comprehensive overview into a more pragmatic and hands-on tool for practice (Figure 5). Throughout the implementation process, implementors should address these factors in their strategy, and should continuously monitor the effectiveness of their strategy to improve it accordingly.[91]

Therefore, awareness of the implementation factors requires additional evidence on *how* to adequately address them.[91, 92] A suggestion for how to address the critical factors 'compatibility' and 'understanding of needs of local users', is developing, testing, and disseminating "homegrown" interventions.[93] This was done in another FRESH AIR study by conducting an intial explorative mixed-method rapid assessment of the local context.[94] The results of this assessment informed implementation strategies for improved cookstove interventions in Uganda, Vietnam and Kyrgyzstan.[95] First, the context assessment revealed that communities and their health workers poorly understood the risk of household air pollution and therefore felt no need for change. Hence, the intervention was preceded by an awareness-raising programme. Second, the rapid assessment helped to identify the relevant influential stakeholders in the settings (e.g. village leaders, district health officers). These stakeholders were then involved in the design of the implementation strategy, which ensured high compatibility of the strategy with the local reality, and engaged the stakeholders (the third critical factor) for the subsequent delivery.[96]

A creative example of addressing the fourth critical factor, lack of access to knowledge and information and skilled staff, could be introducing task-sharing between physician and non-physician health workers. This proved to be effective in lowering blood pressure in LMICs.[97] The fifth critical factor, resource availability, can be particularly challenging to address. One included study reported that workshop facilitators overcame the barrier of transportation costs by ride-sharing and delivering several sessions per visit to reduce the number of visits.[61] Reducing the impact of the lack of resources generally requires innovative system strengthening.[16]

Overall, opinions on how to address implementation factors most effectively turned out to be highly heterogeneous among experts;[98] additional how-to evidence is required.

Implications for implementation research

Studies that systematically evaluate approaches of how to address implementation factors are needed to provide solid and detailed evidence for future initiatives. We are currently working on part two of this review, which focuses on the implementation of clean cooking interventions. However, we argue that future studies should also focus on topics beyond tobacco and clean cooking, such as personalised asthma action plans or pulmonary rehabilitation.[85] The studies included in this review consistently missed economic evaluations, so we recommend future studies to include those.[99] Furthermore, results from the critical appraisal of the studies showed that research quality could generally benefit from more standardised methods and more structured reporting of e.g. context characteristics, implementation strategies, and their conduct. These and additional recommendations are further outlined in an article on improving health-care provider practices for LMICs,[91] and in the STandards for Reporting Implementation Studies.[86]

Implications for practice

Guiding implementation processes by evidence-informed implementation strategies could enhance implementation success. Successful implementation can substantially increase interventions' effectiveness.[17] This could, in turn, optimise the use of already-scarce resources and decrease the high direct and indirect costs associated with CRD in LMICs.[100, 101] Above all, implementation success could improve health outcomes.

Conclusion

In this study, we systematically searched the literature for factors critical to the successful implementation of lung health interventions. We meta-synthesised the factors' level of evidence and developed an implementation tool for practice. Priority for future implementors should be to understand needs of local users, ensure compatibility of the intervention with the local context, engage influential stakeholders, facilitate adequate access to knowledge and information, and secure sufficient resources. Use of the FRESH AIR Implementation Tool could facilitate policymakers, non-governmental organizations, practitioners, researchers, and community members to design evidence-

based, tailored implementation strategies to enhance implementation success. This could hence optimise the use of already scarce resources and, ultimately, improve health outcomes.

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References

1. World Health Organization. Chronic respiratory diseases. 2018 [cited; Available from: http://www.who.int/respiratory/en/
2. World Health Organization. Global Surveillance, prevention and control of chronic respiratory diseases: a comprehensive approach; 2007.
3. Salvi S. The silent epidemic of COPD in Africa. *Lancet Glob Health* 2015: 3(1): e6-7.
4. FitzGerald JM, Al Efraij K. Asthma in low-income and middle-income countries: an urgent call to action. *Thorax* 2018: 73(10): 898-899.
5. Halpin DMG, Celli BR, Criner GJ, Frith P, Lopez Varela MV, Salvi S, Vogelmeier CF, Chen R, Mortimer K, Montes de Oca M, Aisanov Z, Obaseki D, Decker R, Agusti A. It is time for the world to take COPD seriously: a statement from the GOLD board of directors. *Eur Respir J* 2019: 54(1).
6. Pleasants RA, Riley IL, Mannino DM. Defining and targeting health disparities in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2016: 11: 2475-2496.
7. Townend J, Minelli C, Mortimer K, Obaseki DO, Al Ghobain M, Cherkaski H, Denguezli M, Gunesekera K, Hafizi H, Koul PA, Loh LC, Nejjari C, Patel J, Sooronbayev T, Buist SA, Burney PGJ. The association between chronic airflow obstruction and poverty in 12 sites of the multinational BOLD study. *Eur Respir J* 2017: 49(6).
8. Martinez FD. Early-Life Origins of Chronic Obstructive Pulmonary Disease. *N Engl J Med* 2016: 375(9): 871-878.
9. Brakema EA, van Gemert FA, van der Kleij R, Salvi S, Puhan M, Chavannes NH, collaborators FA. COPD's early origins in low-and-middle income countries: what are the implications of a false start? *NPJ Prim Care Respir Med* 2019: 29(1): 6.
10. Sood A, Assad NA, Barnes PJ, Churg A, Gordon SB, Harrod KS, Irshad H, Kurmi OP, Martin WJ, 2nd, Meek P, Mortimer K, Noonan CW, Perez-Padilla R, Smith KR, Tesfaigzi Y, Ward T, Balmes J. ERS/ATS workshop report on respiratory health effects of household air pollution. *Eur Respir J* 2018: 51(1).
11. Beran D, Zar HJ, Perrin C, Menezes AM, Burney P, Forum of International Respiratory Societies working group c. Burden of asthma and chronic obstructive pulmonary disease and access to essential medicines in low-income and middle-income countries. *Lancet Respir Med* 2015: 3(2): 159-170.
12. Gordon SB, Bruce NG, Grigg J, Hibberd PL, Kurmi OP, Lam KB, Mortimer K, Asante KP, Balakrishnan K, Balmes J, Bar-Zeev N, Bates MN, Breysse PN, Buist S, Chen Z, Havens D, Jack D, Jindal S, Kan H, Mehta S, Moschovis P, Naeher L, Patel A, Perez-Padilla R, Pope D, Rylance J, Semple S, Martin WJ, 2nd. Respiratory risks from household air pollution in low and middle income countries. *Lancet Respir Med* 2014: 2(10): 823-860.
13. Torres-Duque CA. Poverty cannot be inhaled and it is not a genetic condition. How can it be associated with chronic airflow obstruction? *Eur Respir J* 2017: 49(6).
14. Thomas E, Wickramasinghe K, Mendis S, Roberts N, Foster C. Improved stove interventions to reduce household air pollution in low and middle income countries: a descriptive systematic review. *BMC Public Health* 2015: 15: 650.

15. Dogar O, Elsey H, Khanal S, Siddiqi K. Challenges of integrating tobacco cessation interventions in TB programmes: Case studies from Nepal and Pakistan. *Journal of Smoking Cessation* 2016: 11(2): 108-115.
16. Mendis S, Al Bashir I, Dissanayake L, Varghese C, Fadhil I, Marhe E, Sambo B, Mehta F, Elsayad H, Sow I, Algoe M, Tennakoon H, Truong LD, Lan le TT, Huiuinato D, Hewageegana N, Fahal NA, Mebrhatu G, Tshering G, Chestnov O. Gaps in capacity in primary care in low-resource settings for implementation of essential noncommunicable disease interventions. *Int J Hypertens* 2012: 2012: 584041.
17. Durlak JA, DuPre EP. Implementation matters: a review of research on the influence of implementation on program outcomes and the factors affecting implementation. *Am J Community Psychol* 2008: 41(3-4): 327-350.
18. Damschroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci* 2009: 4: 50.
19. Burnes B. Emergent change and planned change u competitors or allies?: The case of XYZ construction. *International Journal of Operations & Production Management* 2004: 24(9): 886-902.
20. Bensch G, Grimm M, Peters J. Why do households forego high returns from technology adoption? Evidence from improved cooking stoves in Burkina Faso. *Journal of Economic Behavior & Organization* 2015: 116: 187-205.
21. Clark S, Carter E, Shan M, Ni K, Niu H, Tseng JTW, Pattanayak SK, Jeuland M, Schauer JJ, Ezzati M, Wiedinmyer C, Yang X, Baumgartner J. Adoption and use of a semi-gasifier cooking and water heating stove and fuel intervention in the Tibetan Plateau, China. *Environ Res Lett* 2017: 12(7): 11.
22. El Tayeb Muneer S, Mukhtar Mohamed el W. Adoption of biomass improved cookstoves in a patriarchal society: an example from Sudan. *The Science of the total environment* 2003: 307(1-3): 259-266.
23. Jagger P, Jumbe C. Stoves or Sugar? Willingness to Adopt Improved Cookstoves in Malawi. *Energy policy* 2016: 92: 409-419.
24. Namagembe A, Muller N, Scott LM, Zwisler G, Johnson M, Arney J, Charron D, Mugisha E. Factors influencing the acquisition and correct and consistent use of the top-lit updraft cookstove in Uganda. (Special Issue: Advancing communication and behavior change strategies for cleaner cooking.). *Journal of Health Communication: International Perspectives* 2015: 20(Suppl. 1): 76-83.
25. Brakema EA, van der Kleij RM, Vermond D, van Gemert FA, Kirenga B, Chavannes NH, collaborators FA. Let's stop dumping cookstoves in local communities. It's time to get implementation right. *NPJ Prim Care Respir Med* 2020: 30(1): 3.
26. Peters DH, Adam T, Alonge O, Agyepong IA, Tran N. Implementation research: what it is and how to do it. *BMJ* 2013: 347: f6753.
27. Rogers E. Diffusion of Innovations. 5th ed ed. Free Press: New York 2003.
28. Grol R, Grimshaw J. From best evidence to best practice: effective implementation of change in patients' care. *Lancet* 2003: 362(9391): 1225-1230.
29. Baker R, Camosso-Stefinovic J, Gillies C, Shaw EJ, Cheater F, Flottorp S, Robertson N, Wensing M, Fiander M, Eccles MP, Godycki-Cwirko M, van Lieshout J, Jager C. Tailored interventions to address determinants of practice. *Cochrane Database Syst Rev* 2015(4): CD005470.
30. Mackay J. The role of research on the development and implementation of policy. *Nicotine & Tobacco Research* 2013: 15(4): 757-760.
31. Ahmad N, Boutron I, Dechartres A, Durieux P, Ravaud P. Geographical representativeness of published and ongoing randomized controlled trials. The example of: Tobacco consumption and HIV infection. *PLoS One* 2011: 6(2): e16878.
32. Siddiqi K, Newell J, Robinson M. Getting evidence into practice: what works in developing countries? *Int J Qual Health Care* 2005: 17(5): 447-454.

33. Langer A, Diaz-Olavarrieta C, Berdichevsky K, Villar J. Why is research from developing countries underrepresented in international health literature, and what can be done about it? *Bull World Health Organ* 2004: 82(10): 802-803.
34. Chamberlain C, O'Mara-Eves A, Porter J, Coleman T, Perlen SM, Thomas J, McKenzie JE. Psychosocial interventions for supporting women to stop smoking in pregnancy. *Cochrane Database Syst Rev* 2017: 2: CD001055.
35. Martin K, Mullan Z, Horton R. Overcoming the research to policy gap. *Lancet Glob Health* 2019: 7 Suppl 1: S1-S2.
36. Ridde V. Need for more and better implementation science in global health. *BMJ Glob Health* 2016: 1(2): e000115.
37. Singh SJ, Halpin DMG, Salvi S, Kirenga BJ, Mortimer K. Exercise and pulmonary rehabilitation for people with chronic lung disease in LMICs: challenges and opportunities. *Lancet Respir Med* 2019: 7(12): 1002-1004.
38. Cragg L, Williams S, Chavannes NH. FRESH AIR: an implementation research project funded through Horizon 2020 exploring the prevention, diagnosis and treatment of chronic respiratory diseases in low-resource settings. *NPJ Prim Care Respir Med* 2016: 26: 16035.
39. Higgins JPT GS. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0.
40. Noyes J BA, Cargo M, Flemming K, Harden A, Harris J, Garside R, Hannes K, Pantoja T, Thomas J;. Chapter 21: Qualitative evidence. *In:* Cochrane; In: Higgins JPT TJ, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). , ed. Cochrane Handbook for Systematic Reviews of Interventions version 60 (updated July 2019), 2019.
41. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009: 339: b2535.
42. World Bank. World Bank list of economies - World Bank country and lending groups. 2017 [cited 1 Jul 2019; Available from: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups
43. Rosella L, Bowman C, Pach B, Morgan S, Fitzpatrick T, Goel V. The development and validation of a meta-tool for quality appraisal of public health evidence: Meta Quality Appraisal Tool (MetaQAT). *Public Health* 2016: 136: 57-65.
44. Critical Appraisal Skills Programme. CASP (Qualitative and Cohort) Checklist. 2019 [cited 1 Jul 2017]; Available from: https://casp-uk.net/casp-tools-checklists/
45. Dixon-Woods M AS, Young B, Jones D and Sutton A,. Integrative approaches to qualitative and quantitative evidence: NHS Health Development Agency; 2004.
46. Lewin S, Glenton C, Munthe-Kaas H, Carlsen B, Colvin CJ, Gulmezoglu M, Noyes J, Booth A, Garside R, Rashidian A. Using qualitative evidence in decision making for health and social interventions: an approach to assess confidence in findings from qualitative evidence syntheses (GRADE-CERQual). *PLoS Med* 2015: 12(10): e1001895.
47. Aghi M, Nagler EM, Lando H, Pednekar M, Gupta PC, Sorensen G. Training lay interventionists to support tobacco cessation among teachers in India. *International Journal of Health Promotion & Education* 2016: 54(6): 304-317.
48. Pawar P, Nagler E, Gupta P, Stoddard A, Lando H, Shulman L, Pednekar M, Kasisomayajula V, Aghi M, Sinha D, Sorensen G. Tracking intervention delivery in the 'Tobacco-Free Teachers/Tobacco-Free Society' program, Bihar, India. Health education research, 2015; pp. 731-741.
49. Castaldelli-Maia JM, da Silva NR, Campos MRD, Moura HF, Zabert G, Champagne BM, Kemper KE, Hays JT. Implementing evidence-based smoking cessation treatment in psychosocial care units (CAPS) in Brazil. *International Journal of Social Psychiatry* 2017: 63(8): 669-673.
50. Cruvinel E, Richter KP, Bastos RR, Ronzani TM. Screening and brief intervention for alcohol and other drug use in primary care: associations between organizational climate and practice. *Addiction science & clinical practice* 2013: 8: 4.

51. Medeiros PFP, Cruz JI, Schneider DR, Sanudo A, Sanchez ZM. Process evaluation of the implementation of the Unplugged Program for drug use prevention in Brazilian schools. *Subst/ Abus Treatment Prev Pol* 2016: 11: 11.
52. Pereira AP, Paes AT, Sanchez ZM. Factors associated with the implementation of programs for drug abuse prevention in schools. *Revista de saude publica* 2016: 50: 44.
53. Portes LH, Campos EMS, Teixeira MTB, Caetano R, Ribeiro LC. Actions geared to tobacco control: a review of their implementation in Primary Health Care. *Ciencia & Saude Coletiva* 2014: 19(2): 439-448.
54. Ossip DJ, Diaz S, Quinones Z, McIntosh S, Dozier A, Chin N, Weber E, Holderness H, Torres E, Bautista A, Sanchez JJ, Avendano E, De Ver Dye T, McDonald P, Bianco E. Lessons Learned from Twelve Years of Partnered Tobacco Cessation Research in the Dominican Republic. *J Smok Cessat* 2016: 11(2): 99-107.
55. Marsiglia F, Booth J, Ayers S, Nuño-Gutierrez B, Kulis S, Hoffman S. Short-term effects on substance use of the keepin' it real pilot prevention program: linguistically adapted for youth in Jalisco, Mexico. Prevention science, 2014; pp. 694-704.
56. Ishaak F, de Vries NK, van der Wolf K. Test implementation of a school-oriented drug prevention program "Study without Drugs": pre- and post-testing for effectiveness. *BMC Public Health* 2014: 14: 590.
57. Sodhi S, Banda H, Kathyola D, Joshua M, Richardson F, Mah E, MacGregor H, Kanike E, Thompson S, Fairall L, Bateman E, Zwarenstein M, Schull MJ. Supporting middle-cadre health care workers in Malawi: lessons learned during implementation of the PALM PLUS package. (Special Issue: Uptake and impact of research for evidence-based practice: lessons from the Africa Health Systems Initiative's research component.). *BMC Health Services Research* 2014: 14(Suppl. 1).
58. Bheekie A, Buskens I, Allen S, English R, Mayers P, Fairall L, Majara B, Bateman ED, Zwarenstein M, Bachmann M. The Practical Approach to Lung Health in South Africa (PALSA) intervention: respiratory guideline implementation for nurse trainers. *International nursing review* 2006: 53(4): 261-268.
59. Malan Z, Mash R, Everett-Murphy K. Qualitative evaluation of primary care providers experiences of a training programme to offer brief behaviour change counselling on risk factors for non-communicable diseases in South Africa. *BMC family practice* 2015: 16: 101.
60. Mash B, Rhode H, Pather M, Ainslie G, Irusen E, Bheekie A, Mayers P. Evaluation of the asthma guideline implementation project in the Western Cape, South Africa. *Current Allergy and Clinical Immunology* 2010: 23(4): 154-161.
61. Bteddini D, Afifi R, Haddad P, Jbara L, Alaouie H, Al Aridi L, Mahfoud Z, Al Mulla A, Nakkash R. Process evaluation and challenges of implementation of a school based waterpipe tobacco smoking prevention program for teens in Lebanon. *Tobacco Prevention & Cessation* 2017: 3.
62. Asfar T, Ward KD, Al-Ali R, Maziak W. Building Evidence-Based Tobacco Treatment in the Eastern Mediterranean Region: Lessons Learned by the Syrian Center for Tobacco Studies. *J Smok Cessat* 2016: 11(2): 116-123.
63. Aldinger C, Zhang XW, Liu LQ, Guo JX, Yu Sen H, Jones J. Strategies for implementing Health-Promoting Schools in a province in China. *Promotion & education* 2008: 15(1): 24-29.
64. Aldinger C, Zhang XW, Liu LQ, Pan XD, Yu SH, Jones J, Kass J. Changes in attitudes, knowledge and behavior associated with implementing a comprehensive school health program in a province of China. *Health education research* 2008: 23(6): 1049-1067.
65. Wang JF, Ma SJ, Mei CZ, Xu XF, Wang CP, Yang GH. Exploring barriers to implementation of smoking policies: A qualitative study on health professionals from three county-level hospitals. *Biomedical and Environmental Sciences* 2008: 21(3): 257-263.
66. Xiao D, Wang C, Chen H, Hajek P. Making hospitals in China smoke-free: a prospective study of implementing the new standard. *Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco* 2013: 15(12): 2076-2080.

67. Ziedonis DM, Wang X, Li T, Kim SS, Tonelli ME, Li S, Kalman D. Addressing tobacco through organizational change in a hospital-based mental health center in china: The intervention and lessons learned in a pilot implementation project. *Journal of Dual Diagnosis* 2012: 8(2): 148-157.
68. Chatterjee N, Patil D, Kadam R, Fernandes G. The Tobacco-Free Village Program: Helping Rural Areas Implement and Achieve Goals of Tobacco Control Policies in India. *Global health, science and practice* 2017.
69. Goenka S, Tewari A, Arora M, Stigler MH, Perry CL, Arnold JP, Kulathinal S, Reddy KS. Process evaluation of a tobacco prevention program in Indian schools--methods, results and lessons learnt. *Health education research* 2010: 25(6): 917-935.
70. Nagler EM, M. S. Pednekar, K. Viswanath, D. N. Sinha, M. B. Aghi, C. R. Pischke, C. B. Ebbeling, H. A. Lando, P. C. Gupta, and G. C. Sorensen. Designing in the Social Context: Using the Social Contextual Model of Health Behavior Change to Develop a Tobacco Control Intervention for Teachers in India. *Health Education Research* 2013: 28 (1): 113-129.
71. Nichter M, Nichter M, Muramoto M, Project Quit Tobacco I. Project Quit Tobacco International: laying the groundwork for tobacco cessation in low- and middle-income countries. *Asia Pac J Public Health* 2010: 22(3 Suppl): 181S-188S.
72. Perry C, Stigler M, Arora M, Reddy K. Prevention in translation: tobacco use prevention in India. Health promotion practice, 2008; pp. 378-386.
73. Persai D, Panda R, Gupta A. Examining Implementation of Tobacco Control Policy at the District Level: A Case Study Analysis from a High Burden State in India. *Advances in preventive medicine* 2016: 2016: 4018023.
74. Prasodjo R, Musadad DA, Muhidin S, Pardosi J, Silalahi M. Advocate program for healthy traditional houses, Ume Kbubu, in a Timor community: preserving traditional behavior and promoting improved health outcomes. *Journal of health communication* 2015: 20 Suppl 1: 10-19.
75. Melson E, Bridle C, Markham W. Pragmatic pilot cluster randomised control trial of a school-based peer-led anti-smoking intervention for 13-14 year olds in Malaysia: Process evaluation. *Health Education* 2017: 117(6): 599-616.
76. Elsey H, Khanal S, Manandhar S, Sah D, Baral SC, Siddiqi K, Newell JN. Understanding implementation and feasibility of tobacco cessation in routine primary care in Nepal: a mixed methods study. *Implement Sci* 2016: 11: 104.
77. Mehanni S, Jha D, Kumar A, Choudhury N, Dangal B, Deukmedjian G, Dhungana SK, Gauchan B, Gupta TK, Halliday S, Kalaunee SP, Mahar R, Poudel S, Raut A, Schwarz R, Singh DR, Thapa A, Thapa R, Wong L, Maru D, Schwarz D. Implementing a quality improvement initiative for the management of chronic obstructive pulmonary disease in rural Nepal. *BMJ Open Quality* 2019: 8 (1) (no pagination)(e000408).
78. Khan MA, Khan MA, Walley JD, Khan N, Sheikh FI, Ali S, Salahuddin E, King R, Khan SE, Manzoor F, Khan HJ. Feasibility of delivering integrated COPD-asthma care at primary and secondary level public healthcare facilities in Pakistan: a process evaluation. *BJGP Open* 2019: 3(1): bjgpopen18X101632.
79. McAlister A, Gumina T, Urjanheimo E, Laatikainen T, Uhanov M, Oganov R. Promoting smoking cessation in Russian Karelia: a 1-year community-based program with quasi-experimental evaluation. Health promotion international, 2000; pp. 109-112.
80. Assanangkornchai S, Balthip Q, Edwards JG. Implementing the Alcohol, Smoking, Substance Involvement Screening Test and linked brief intervention service in primary care in Thailand. *Journal of public health (Oxford, England)* 2014: 36(3): 443-449.
81. Rosati MJ, Cupp PK, Chookhare W, Miller BA, Byrnes HF, Fongkaew W, Vanderhoff J, Chamratrithirong A, Rhucharoenpornpanich O, Atwood KA. Successful implementation of Thai Family Matters: strategies and implications. *Health promotion practice* 2012: 13(3): 355-363.
82. Vitavasiri C, Pausawasdi S. Implementation of 100% smoke-free hospital in Thailand. *Journal of the Medical Association of Thailand = Chotmaihet thangphaet* 2010: 93(7): 860-864.

83. Groth-Marnat G, Leslie S, Renneker M. Tobacco control in a traditional Fijian village: Indigenous methods of smoking cessation and relapse prevention. *Social Science & Medicine* 1996: 43(4): 473-477.
84. Luyckx VA, Reis A, Maher D, Vahedi M. Highlighting the ethics of implementation research. *Lancet Glob Health* 2019: 7(9): e1170-e1171.
85. The Lancet Respiratory M. Smoking cessation efforts should target LMICs. *Lancet Respir Med* 2019: 7(9): 721.
86. Pinnock H, Barwick M, Carpenter CR, Eldridge S, Grandes G, Griffiths CJ, Rycroft-Malone J, Meissner P, Murray E, Patel A, Sheikh A, Taylor SJ, Sta RIG. Standards for Reporting Implementation Studies (StaRI) Statement. *BMJ* 2017: 356: i6795.
87. Puzzolo E, Pope D, Stanistreet D, Rehfuess EA, Bruce NG. Clean fuels for resource-poor settings: A systematic review of barriers and enablers to adoption and sustained use. *Environmental research* 2016: 146: 218-234.
88. Rehfuess EA, Puzzolo E, Stanistreet D, Pope D, Bruce NG. Enablers and barriers to large-scale uptake of improved solid fuel stoves: a systematic review. *Environmental health perspectives* 2014: 122(2): 120-130.
89. Greenhalgh T, Taylor R. Papers that go beyond numbers (qualitative research). *BMJ* 1997: 315(7110): 740-743.
90. Movsisyan A, Arnold L, Evans R, Hallingberg B, Moore G, O'Cathain A, Pfadenhauer LM, Segrott J, Rehfuess E. Adapting evidence-informed complex population health interventions for new contexts: a systematic review of guidance. *Implement Sci* 2019: 14(1): 105.
91. Rowe AK, Rowe SY, Peters DH, Holloway KA, Chalker J, Ross-Degnan D. Effectiveness of strategies to improve health-care provider practices in low-income and middle-income countries: a systematic review. *Lancet Glob Health* 2018: 6(11): e1163-e1175.
92. Daivadanam M, Ingram M, Sidney Annerstedt K, Parker G, Bobrow K, Dolovich L, Gould G, Riddell M, Vedanthan R, Webster J, Absetz P, Molsted Alvesson H, Androutsos O, Chavannes N, Cortez B, Devarasetty P, Fottrell E, Gonzalez-Salazar F, Goudge J, Herasme O, Jennings H, Kapoor D, Kamano J, Kasteleyn MJ, Kyriakos C, Manios Y, Mogulluru K, Owolabi M, Lazo-Porras M, Silva W, Thrift A, Uvere E, Webster R, van der Kleij R, van Olmen J, Vardavas C, Zhang P, Concepts G, Contexts working g. The role of context in implementation research for non-communicable diseases: Answering the 'how-to' dilemma. *PLoS One* 2019: 14(4): e0214454.
93. Ward KD. Tobacco intervention research in low- and middle-income countries: lessons learned and future directions. *J Smok Cessat* 2016: 11(2): 61-64.
94. Beebe J. Basic Concepts and Techniques of Rapid Appraisal. *Human Organization* 1995: 54(1).
95. van Gemert F, de Jong C, Kirenga B, Musinguzi P, Buteme S, Sooronbaev T, Tabyshova A, Emilov B, Mademilov M, Le An P, Quynh NN, Dang TN, Hong L, Chartier R, Brakema EA, van Boven JFM, Fresh AIR. Effects and acceptability of implementing improved cookstoves and heaters to reduce household air pollution: a FRESH AIR study. *NPJ Prim Care Respir Med* 2019: 29(1): 32.
96. Vardavas CI, Kyriakos CN, Fernandez E, Bamidis P, Siddiqi K, Chavannes NH, van der Kleij R, Parker G, Radu-Loghin C, Ward B, Berkouk K. H2020 funding for respiratory research: scaling up for the prevention and treatment of lung diseases. *Eur Respir J* 2019: 54(3).
97. Anand TN, Joseph LM, Geetha AV, Prabhakaran D, Jeemon P. Task sharing with non-physician health-care workers for management of blood pressure in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet Glob Health* 2019: 7(6): e761-e771.
98. Waltz TJ, Powell BJ, Fernandez ME, Abadie B, Damschroder LJ. Choosing implementation strategies to address contextual barriers: diversity in recommendations and future directions. *Implement Sci* 2019: 14(1): 42.
99. Powell BJ, Fernandez ME, Williams NJ, Aarons GA, Beidas RS, Lewis CC, McHugh SM, Weiner BJ. Enhancing the Impact of Implementation Strategies in Healthcare: A Research Agenda. *Front Public Health* 2019: 7: 3.

100. Brakema EA, Tabyshova A, van der Kleij R, Sooronbaev T, Lionis C, Anastasaki M, An PL, Nguyen LT, Kirenga B, Walusimbi S, Postma MJ, Chavannes NH, van Boven JFM, collaborators FA. The socioeconomic burden of chronic lung disease in low-resource settings across the globe - an observational FRESH AIR study. *Respir Res* 2019: 20(1): 291.
101. Horvath I, Barry M, Brusselle G, Burghuber OC, Bush A, Robalo Cordeiro C, Gaga M, Gratziou C, Saraiva I, Stolz D, Troosters T, Welte T, Migliori GB, Joos G. The European Respiratory Society's 10 Principles for Lung Health. *Eur Respir J* 2018: 52(5).

Figure 1. Tools used in each phase

Meta-QAT = Meta Quality Appraisal Tool; CASP = Critical Appraisal Skills Programme; CFIR = Consolidated Framework for Implementation Research; GRADE-CERQual = Grading of Recommendations Assessment, Development and Evaluation-Confidence in the Evidence from Reviews of Qualitative research

[1] Rosella, L. *et al.* The development and validation of a meta-tool for quality appraisal of public health evidence: Meta Quality Appraisal Tool (MetaQAT). *Public Health* **136**, 57-65, (2016).
[2] Critical Appraisal Skills Programme. *CASP (Qualitative and Cohort) Checklist.* https://casp-uk.net/casp-tools-checklists/ (2019).
[3] Higgins JPT GS. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0.
[4] Evaluation of a large-scale weight management program using the consolidated framework for implementation research (CFIR) Laura J Damschroder* and Julie C Lowery.
[5] Damschroder, L. J. *et al.* Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. *Implement Sci* **4**, 50, (2009).
[6] A systematic review of implementation frameworks of innovations in healthcare and resulting generic implementation framework (Moullin).
[7] Lewin, S. *et al.* Using qualitative evidence in decision making for health and social interventions: an approach to assess confidence in findings from qualitative evidence syntheses (GRADE-CERQual). *PLoS Med* **12**, e1001895, (2015).
[8] Dixon-Woods M, A. S., Young B, Jones D and Sutton A,. Integrative approaches to qualitative and quantitative evidence. (NHS Health Development Agency, 2004).

Figure 2. Flow diagram of screening process

Figure 3. Study settings and interventions

Symbols with 2 colours indicate the study covered both interventions. Half a symbol means half of the study was conducted in this setting, and the other half in another setting.

Figure 4. Full overview of implementation factors per domain, and the relative level of evidence for the factor

Figure 5. FRESH AIR Implementation Tool

*These suggestions are based on the literature specific interventions targeting chronic respiratory disease in low-and middle-income countries, and on additional, general implementation literature. See Appendix 7 for recommended use and details on references.